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(54) Title: PROCESS FOR PREPARING PVP-IODINE PRODUCT

(57) Abstract

A proces for preparing a water-insoluble or water-soluble PVP-iodine product which comprises intimately mixing water-insoluble PVP or water-soluble PVP having a K-value of 10-20, about 10 to 20 % by weight of iodine powder and about 0.05 to 1 % by weight of isopropanol, heating the reaction mixture at a mixing temperature of room temperature to about 30-60 °C for about 0.5 to 6 hours, and heating the mixture at a reaction temperature of about 65 to 98 °C for about 10-24 hours, generally at least 18 hours, to form a stable, uniform, free-flowing powder.

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PROCESS FOR PREPARING PVP-IODINE PRODUCT

A process is described herein for preparing a uniform, free-flowing water-insoluble or water soluble PVP-iodine product which comprises intimately mixing water-insoluble or water soluble PVP of K-value 10-20, about 10 to 20% by weight iodine powders and about 0.05 to 1% by weight of isopropanol, heating the reaction mixture at a mixing temperature of from room temperature to about 30-60°C. for about 0.5 to 6 hours, until the reactants disappear as a separate phase, and heating the mixture at a reaction temperature of about 65 to 98°C. for about 10-24 hours, generally at least 18 hours, thereby forming a uniform, free-flowing powder.

The water-insoluble and water-soluble PVP starting materials are available from International Specialty Products Inc. (ISP).

The process of preparing water-insoluble PVP-iodine involves preparing reaction powders by intimately mixing crospovidone, about 10 to 20% by wt. of iodine and about 0.5 to 1% by wt. of isopropanol, heating at a mixing temperature of about 30-60°C. for about 0.5-6 hours, and then heating the mixture at a reaction temperature of about 75-98°C. for about 10-24 hours, to form a uniform, free-flowing powder having an available iodine content of about 9-13% and an iodide content of about 4-6%.

Representative reaction mixtures, process conditions and properties of the reaction product obtained by such process are shown in the TABLE below.

TABLE 1

	Suitable	Preferred	Optimum
Reaction Mixture and Process Conditions			
PVP*	80-90	81-85	83
I_2 (% by wt.)	10-20	15-19	17
Isopropanol (% by wt.)	0.05-1	0.1-0.5	0.2
Mixing temp. (°C.)	30-60	35-55	45
Mixing time (hrs.)	0.5-6	1-5	3
Reaction temp (°C.)	75-98	85-95	90
Reaction period (hrs.)	10-24	12-20	16
Reaction Product			
Avail. I_2 (% by wt.)	9-13	10-12	11
Iodide (% by wt.)	4-6	4.5-5.5	5
Moisture content (% by wt.)	1-5	1.5-3.5	2

The invention will now be illustrated by the following example.

* Polyplasdone® (ISP)

EXAMPLE 1

50 g. of Polyplasdone® (ISP) 10 g. of iodine (Japan crushed, 99.5%), and 0.12 g. isopropanol are charged into a pint-wide mouth glass jar with a Teflon-lined lid, and having a Teflon plate and wall indentations for effective baffling. The charged jars were placed in a forced air oven equipped with a motor driven rotary cage to allow rotation of the jars at 40 rpm. The reaction mixture in the jars were hand mixed for about 1/2 minute to disperse the iodine therein, and then the isopropanol was added dropwise, mixed again for 1/2 minute, rotated in the oven at 45°C. for 3 hours, and then heated at 90°C. for 16 hours. A yellow-brown, free-flowing powder was obtained. The available iodine content of the product was 12.15%; the iodide content was 4.45%; and the moisture content was 2.37%. The product lost was less than 10% iodine after heating at 75°C. for 6 hours.

The water-soluble PVP-iodine product of the invention is prepared by reacting 80-90% by wt. water-soluble PVP with 10-20% by wt. iodine at a temperature of about 65-85°C., preferably about 75°C., for a period of at least about 18 hours, and, in the presence of a small amount, e.g. 0.1-0.2, preferably, 0.2%, of isopropanol.

The parameters of the process of the invention, and the product produced thereby are summarized in the Table below.

TABLE 2

Reaction Mixture and Process Conditions	Ranges Suitable	Preferred	Optimum
Water-Soluble PVP (K = 10-20)	80-90	81-85	83
I_2 (% by wt.)	10-20	15-19	17
Isopropanol (% by wt.)	0.05-1	0.1-0.5	0.2
Room Temperature Mixing (hrs.)	3-16	5-10	7.5
Reaction Temp (°C.)	65-85	70-80	75
Reaction Time (hrs.) at least	12	> 16	16-22
Reaction Product			
K-Value	10-20	13-17	15
Avail I_2 (% by wt.)	9-13	10.5-11.5	11
Iodide (% by wt.)	4-6	4.5-5.5	5
Partition Coefficient	>150	180-220	200

EXAMPLE 2

60 g. of water-soluble PVP (K-value 12-20) powder, 12.0 g. of iodine powder and 0.144 g. of isopropanol were mixed in a jar and the mixture was rotated with a motor driven rotary cage at 40 rpm at room temperature for 3-16 hours. The iodine powders disappeared as a separate phase

and the reaction mixture was a uniform, nearly black powder which was flowable. This mixture then was rotated continuously at 75°C. for 22 hours. The product was a uniform, free-flowing, reddish-brown powder. The available iodine content was 10.99%, the iodide content was 4.80%; and the moisture content was 3.14%.

Stability was measured by % iodine loss after 6 hours at 75°C. from a 1% available iodine solution, only 3.64% of available iodine was lost. The partition coefficient of the product was 148.

WHAT IS CLAIMED IS:

1. A process for preparing a water-insoluble or water-soluble PVP-iodine product which comprises intimately mixing about 80 to about 90% by wt. of water-insoluble or water-soluble PVP, having a K-value of about 10-20, about 10 to about 20% by wt. iodine powders and about 0.05 to about 1% by wt. of isopropanol, heating the reaction mixture at a mixing temperature of from room temperature to about 30 to about 60°C. for about 0.5 to 6 hours, and heating the mixture at a reaction temperature of about 65 to about 98°C. for about 10 to about 24 hours, thereby forming a stable, uniform, free-flowing powder.

2. A process according to claim 1 wherein the water-insoluble product has an available iodine content of about 9 to about 13% and an iodide content of about 4 to about 6%.

3. A process according to claim 1 wherein iodine is charged in an amount of about 15-19% by wt.

4. A process according to claim 1 wherein isopropanol is charged in an amount of about 0.1-0.5% by wt.

5. A process according to claim 1 wherein said reaction temperature is about 85-95°C. and the reaction time is about 12-20 hours.

6. A process according to claim 1 wh rein the product has an available iodine content of about 10 to 12% and an iodide content of about 4.5 to 5.5%.

7. A process according to claim 1 wherein the mixing temperature is about 35-55°C. and the mixing time is about 1-5 hours.

8. A process according to claim 1 wherein the moisture content of the product is about 1-5% by wt.

9. A process according to claim 1 wherein the iodine charge is 17% by wt., the isopropanol is about 0.2% by wt., the mixing temperature is about 45°C., the mixing time is about 3 hours, the reaction temperature, is about 90°C., the reaction time is about 16 hours, and wherein the reaction product has about 11% by wt. available iodine, about 5% by wt. iodide and about 2% by wt. moisture.

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 31/79; C08F 8/18
US CL :424/78.25; 525/356
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/78.25; 525/356

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 2,706,701 (BELLER ET AL.) 19 April 1955; See column 2.	1- 9
A	US, A, 3,136,755 (GROSSER ET AL.) 09 June 1964; See column 4, lines 44-71.	1-9
A	US, A, 4,113,857 (SHETTY) 12 September 1978; See Abstract.	1-9
A	US, A, 4,214,059 (HOFER) 22 July 1980; See column 1 and 3.	1-9
A	US, A, 4,954,351 (SACKLER ET AL.) 04 September 1990; See column 1.	1-9

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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